stones while receiving lower doses of octreotide than those used in their study.

As none of the patients had had ultrasound examinations before starting treatment we cannot be certain that all the gall stones developed as a result of the octreotide treatment. None the less, the 50% rate of calculi in these patients is considerably higher than would be expected in the general population. The results of recent large epidemiological studies, based on ultrasound screening of random samples of the population, suggest that the overall prevalence of gall stone disease is 11%, with a comparable prevalence in the 40-49 age group (7·9% in men and 14·3% in women).[2,3] Even though it increases with age from 2·1-2·5% in the 18-29 age group to 19·8-25·0% in the 60-69 age group, the prevalence is much lower than for our acromegalic patients treated with octreotide.

There is no evidence that acromegaly itself induces formation of gall stones, but it is known that patients with tumours secreting somatostatin have a high incidence of gall stone disease.[4] It seems likely, therefore, that the greater than expected rate of gall stones in our patients is indeed due to the treatment with somatostatin analogue.

The mechanism whereby octreotide might induce gall stone formation is unknown, but the most obvious explanation is that it prevents meal stimulated release of cholecystokinin from the intestine[5,6] with resultant stasis in the gall bladder.[7] In general, for gall stones to develop three abnormalities must coexist (the so called triple defect[8]): supersaturated bile that is overloaded with cholesterol (or other constituents of gall stones); abnormal nucleation of the supersaturated bile due to an excess of promotors or a deficiency of inhibitors of crystallisation, or both; and gall bladder hypomotility. Occasionally, however, one component may predominate, leading to gall stone formation in the absence of the other two factors. Thus bile stasis associated with impaired gall bladder contractility may be the mechanism for gall stone formation not only in patients treated with octreotide[8] but also in parenterally nourished infants[10] and adults.[11] If gall stone formation induced by octreotide is confirmed this may provide the strongest evidence yet available that the changes in gall bladder motility seen in patients with gall stones[12] may be a primary phenomenon antedating and contributing to gall stone formation, rather than a secondary phenomenon resulting from chronic cholecystitis induced by gall stones. It remains possible, however, that octreotide leads to changes in the composition of bile acids with resultant biliary cholesterol supersaturation[13] (although this suggestion is controversial[14]) secondary to alterations in intestinal motility and gut flora. Alternatively, for reasons unknown, octreotide could in theory affect nucleation of crystals from supersaturated bile.

Although the course of untreated gall stone disease is generally benign,[15] it would seem important to prevent this potential complication of octreotide treatment if possible. Until the putative mechanisms for induced gall stone formation have been examined and defined, however, countermechanisms to prevent this phenomenon cannot logically be postulated. Such studies are now in progress in our departments.

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Needlestick injuries in syringe exchange projects

SIR,—Dr John Strang's letter[1] raises a point that does not seem to have been addressed up to now. The Association for Prevention of Addiction, of which I am chairman, is engaged in counselling drug misusers—including the promotion of harm reduction by advising on proper injection practices—and is shortly to start up a needle exchange project. I have been concerned about proper insurance cover for our workers, both volunteer and paid, in respect of professional indemnity and needlestick injuries. Our coordinator has telephoned most of the London voluntary agencies and found that only two actually have professional indemnity insurance.

The position of those agencies that operate under health authority aegis is secure, for health authorities themselves carry indemnity. But the voluntary agencies are in a vulnerable position, and I think it is essential and urgent that the Department of Health extend this indemnity to all member organisations of the Standing Conference on Drug Abuse.

The level of risk is admittedly low, but in the present climate of fear on the part of insurers it is likely that they will sell cover only at a price and under conditions that would be out of reach for most voluntary agencies.

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1 Strang J. Needlestick injuries in syringe exchange projects. *Br Med J* 1989;**299**:735. (16 September.)

Sweeping away superstition?

SIR,—Ms Diana Lockwood's article, "Sweeping away superstition?"[1] was as misleading as the *Hard News* programme she was writing about (I have made a formal complaint to the Broadcasting Complaints Commission about *Hard News*). I am constantly surprised by the readiness of academics to burst into print.

The most important error Ms Lockwood made was to hint that I had suggested that leprosy is "extremely infectious, with an appreciable risk of transmission occurring by hand to hand contact." I made it very clear that the risk was low. I suggest that Ms Lockwood study the basic textbooks on leprosy. For example, in the current edition of *A Short Textbook of Preventive Medicine for the Tropics* she will find that the authors point out that there are well authenticated cases of patients acquiring the infection after a brief passing contact with a person suffering from leprosy.[2]

My advice to Princess Diana was well meant and honestly based. Ms Lockwood may disagree with my advice but she cannot fault the scientific logic on which it was based.

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Epilepsy in women of childbearing age

SIR,—Dr Michael Saunders's editorial is a welcome and highly sensible discussion of the problems of managing young women with epilepsy who may be considering pregnancy.[1] Though all drugs are potentially teratogenic, treatment with carbamazepine is probably the safest regimen in pregnancy although it may be associated with craniofacial defects and developmental delay.[2] It may not, however, be the most effective drug for many young women and the decision as to whether to use the alternative drug, valproate, in this age group requires careful balancing of the therapeutic benefits against the potential risk of neural tube defects induced by drugs. In this, things may not be so black and white as Dr Saunders suggests.

The higher incidence of fetal abnormalities in pregnancies of women with epilepsy may not solely be due to drug effects: genetic links between abnormalities and epilepsy and effects of seizures during pregnancy possibly have influences.[3] Thus it has recently been suggested that the risk of neural tube defects may be 1-2% for valproate, 0·5-1% for carbamazepine, and 0·3-0·4% for barbiturates and phenytoin.[4]

Dr Saunders recognises that valproate is highly effective in simple absence epilepsy. It is also the most effective antiepileptic drug in other forms of idiopathic generalised epilepsy. Numerically, juvenile myoclonic epilepsy and epilepsy with wakening tonic-clonic seizures, both of which exhibit generalised spike wave in the electroencephalogram, are commoner in women of childbearing age than is simple absence epilepsy. Juvenile myoclonic epilepsy presents a particular management problem. The syndrome is characterised by early morning myoclonus and tonic-clonic seizures with onset in the second decade of life. It is often associated with photosensitivity, and sleep deprivation seems to provoke seizures. Though the syndrome is often unrecognised by British clinicians, it probably accounts for between 4% and 6% of all the epilepsies and a proportionately larger number of patients in the childbearing age group.[5]

The response of this syndrome to other anticonvulsants is often less than optimal, but valproate seems highly effective, resulting in remission in well over 90% of patients. Unfortunately, even after prolonged remissions relapses occur in 90% of patients if valproate withdrawal is attempted. Thus many young women with epilepsy may

depend on valproate for optimal control of their seizures throughout the childbearing years.[5]

It is clearly of enormous importance that women with primary generalised epilepsies are differentiated from those with partial epilepsy, who will be best managed with carbamazepine. They are a group requiring specific counselling of the small risks of valproate to any pregnancy and needing screening of any pregnancy for neural tube defects within the first trimester. Patients themselves can probably best decide whether they wish to take the most effective drug and accept a small risk of neural tube defect or to take a less optimal drug that might be somewhat safer in pregnancy.

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Medical students' electives

SIR,—Dr J M S Pearce puts serious questions about a subject that has several meanings.[1] Multiple electives chosen by the student may make up a whole year of study after a baseline syllabus, as in many American schools. In this country schools design a core curriculum leading to the final MB in keeping with the General Medical Council's guidelines; this is generally conducted on extended home ground, meaning the teaching hospitals and appropriate district hospitals. Students have a single elective period for additional clinical experience under their own initiative. This time is often spent abroad, and the students' plans need the dean's approval.

Students and deans have no difficulty in defending the single elective: it is a valuable complement to core studies, adds a welcome breath to individual talent and freedom, widens horizons, and so on. "Elective" is not a good description of the carefully constructed secondment of students to district hospitals. In this school's short history, beginning with the joint foundation by the NHS and the university of a regional clinical school, East Anglian district hospitals have always been part of our core teaching base. The university appoints a local director of clinical studies, reports are made on each student's stay at the hospital, and we aim to meet once a year to compare notes. The university also gives the title of recognised clinical teacher to consultants who do substantial teaching, and the service increment for teaching is calculated for redirecting funds. Occasionally the university hospital worries that the students are all too keen on their district hospital attachments.[2] There is much to be improved, but Dr Pearce's charges of general laissez faire are not quite fair.

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1 Pearce JMS. Does the student elective achieve its aim? *Br Med J* 1989;**299**:925. (7 October.)
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SIR,—Dr J M S Pearce's interesting article on student electives highlights the rather odd relationship between medical schools and district general hospital consultants.[1] I have just received a communication from the dean of our local medical school informing me that the university will no longer be able to offer a fee for the formal teaching sessions that most of us undertake from time to time in the medical school. The argument used was that the fees are so small that they are not worth having. One must agree that a fee of £15 for two afternoons' work, including a 30 mile round trip each time, is not generous, but it was a nice gesture. I am sure that most peripheral hospital consultants will continue to support the medical schools by formal and informal teaching without remuneration because they enjoy it and feel they have something to offer. In the current climate, however, it is probably unwise of medical schools to plan on this arrangement continuing: the managers of self governing hospitals may not be too enthusiastic about this sort of use of consultant time.

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Serum paraproteins in osteoporosis

SIR,—Dr A L Dolan and colleagues present good evidence to support the investigation of immunoglobulin profile and paraproteinaemia in patients with apparently "simple" osteoporosis.[1] Rather than using immunoelectrophoresis as they suggested, we recommend immunoisoelectric focusing as the appropriate screening method for paraproteins. We have found this to be 10-40 times more sensitive,[2] with a resulting increase in detection rate. More importantly, in the difficult cases of "non-secretory" myeloma highlighted by Dr Dolan and colleagues we have detected monoclonal bands with immunoisoelectric focusing when conventional techniques have failed.[3] This technique can also quantify the paraprotein, thus giving an objective measurement for assessing treatment.[4] We suggest that immunoisoelectric focusing is a useful laboratory adjunct in investigating osteoporosis.

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Osteoporosis and immunosuppression in multiple myeloma

SIR,—Dr A L Dolan and colleagues correctly emphasise the need to investigate hypogammaglobulinaemia in association with osteoporosis so that this presentation of myeloma is not missed.[1] The patient with a crush vertebral fracture (case 2) had the more common presentation of bone pain.[2]

We take issue with the immunological investigations described. In particular, immunoelectrophoresis is not a quantitative technique as suggested in the text nor is it as sensitive as immunofixation.[3] The relatively poor sensitivity of immunoelectrophoresis may result in paraprotein not being detected in so called non-secretory meyloma[4]; this may have been applicable to case 2, in which Bence Jones protein was initially isolated from urine.

Myeloma is not the only cause of a marrow plasmacytosis, and determining the monoclonality of such plasma cells is crucial to the investigation of myeloma; this does not seem to have been undertaken in case 1. Case 2 showed synthesis of κ Bence Jones protein in plasma cells, but the type of the urinary Bence Jones protein was not indicated. Case 2 cannot therefore be considered to be a non-secretory myeloma as a secreted product was identified, albeit on one occasion.

In patients with "simple" osteoporosis and in whom there are no clinical findings suggesting myeloma immunoelectrophoresis is not indicated. If, however, there is clinical suspicion of myeloma, as in case 2, the initial investigations should be high resolution electrophoresis of serum and appropriately concentrated urine with immunochemical quantitation of serum immunoglobulins.

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Persistence of cytomegalovirus in peripheral blood from blood donors

SIR,—Mr Philip Stanier and colleagues report the detection of cytomegalovirus DNA sequences in peripheral blood mononuclear cells by polymerase chain reaction.[1] In a preliminary study we have obtained similar results. Mononuclear cell fractions were separated on Ficoll-Hypaque density gradients, the DNA extracted by standard methods, and cytomegalovirus DNA assayed by polymerase chain reaction.[2] We amplified a 194 nucleotide sequence within the *Hind* III J fragment (that is, within the gene coding for the large structural phosphoprotein, molecular weight 150 000[3]) using primers 20 bases long and probed the reaction products after Southern blotting using an internal fragment of the above sequence 76 bases long labelled with phosphorus-32. IgG antibody specific to cytomegalovirus was assayed by indirect radioimmunoassay.[4] Mononuclear cells from all four seropositive volunteer donors studied and three of four seronegative volunteer donors were positive for cytomegalovirus DNA by polymerase chain reaction, despite the absence of cytomegalovirus viraemia as assayed by isolating the virus.

We and Mr Stanier and coworkers were thus able to detect cytomegalovirus DNA by polymerase chain reaction in peripheral blood mononuclear cells collected from all seropositive and some seronegative volunteer donors. None the less, others have failed to confirm these observations.[5-7] This difference may reflect differing sensitivities of the assays used or contamination of specimens